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(autoluminescence) from human hands measured with an EMCCD camera:
Dependence on time of day, date and individual subject**

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DOI: <https://doi.org/10.19185/matters.2018030000001>

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ZORA URL: <https://doi.org/10.5167/uzh-161846>

Journal Article

Published Version



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Originally published at:

Scholkmann, Felix; van de Kraats, Everine; van Wijk, Roeland; van Wijk, Eduard; van der Greef, Jan (2018). Spatio-temporal dynamics of spontaneous ultra-weak photon emission (autoluminescence) from human hands measured with an EMCCD camera: Dependence on time of day, date and individual subject. *Matters*:1-5.

DOI: <https://doi.org/10.19185/matters.2018030000001>

✉ **Correspondence**
Felix.Scholkmann@usz.ch

🔗 **Disciplines**
Biophysics

🔍 **Keywords**
Ultra-Weak Photon Emission
Autoluminescence
Imaging
Biophotonics

📅 **Type of Observation**
Follow-up

🔗 **Type of Link**
Continuing the storyline

🕒 **Submitted** Jan 25, 2018
📅 **Published** Mar 16, 2018



Triple Blind Peer Review
The handling editor, the reviewers, and the authors are all blinded during the review process.



Full Open Access
Supported by the Velux Foundation, the University of Zurich, and the EPFL School of Life Sciences.



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Spatio-temporal dynamics of spontaneous ultra-weak photon emission (autoluminescence) from human hands measured with an EMCCD camera: Dependence on time of day, date and individual subject

Felix Scholkmann, Everine B van de Kraats, Roeland van Wijk, Eduard P van Wijk, Jan van der Greef

Department of Neonatology, University Hospital Zurich, University of Zurich, Zurich, Research Office for Complex Physical and Biological Systems; Leiden University, Sino-Dutch Centre for Preventive and Personalized Medicine; Leiden University, Sino-Dutch Centre for Preventive and Personalized Medicine, Geldermalsen, The Netherlands, Meluna Research

Abstract

Biological tissue exhibits autoluminescence, i.e. a spontaneous ultra-weak photon emission (UPE) without photoexcitation. In this study, we report UPE measurements on human hands using an electron-multiplying CCD (EMCCD) camera. The images from left and right hands (2 subjects, 10 images in total) were taken on different dates. We observed the following spatio-temporal aspects of the hand UPE images: (i) all images show clearly that human hands exhibit autoluminescence; (ii) there was large variability in the UPE intensity with respect to the factors: time (time of day, date), anatomical location on the hand, and individual subject; (iii) images taken on the same date (but at different times of day) showed a stronger similarity than images of the same subject taken on different dates; (iv) the mean UPE intensity (averaged over 2 regions of interest at the right and left dorsum of the hands) correlated with the time of measurement (lower intensity at around noon). Our study documents the feasibility of UPE imaging of hands with an EMCCD camera and shows that the spatio-temporal variability of the UPE pattern harbours information that seems to be correlated to internal and external factors.

Introduction

Whereas *autofluorescence* of cells and biological tissue is fluorescent light emission due to stimulated light reactions with endogenous fluorophores [1], tissue exhibits also *autoluminescence*, i.e. spontaneous ultra-weak photon emission (UPE) in the ultra-violet to visible/near-infrared spectral range (approx. 200–1300 nm) without photoexcitation [2] [3] [4]. The photon emission associated with autoluminescence is magnitudes lower compared to the case of autofluorescence, challenging the technical detection of this phenomenon. The UPE intensity has generally only an intensity in the order of 10^1 – 10^4 photons/s cm² [5].

The source of the UPE due to autoluminescence is mainly biochemical, i.e. the de-excitation of energetically excited species like atoms and/or molecules to a deeper energy level generating photons [3] [6] [7]. The excited states are generally caused by oxidative reactions involving radical or non-radical reactive oxygen (ROS) and nitrogen (RNS) species that react with several biomolecules like lipids, proteins and nucleic acids. Also, the self-recombination of organic radicals is relevant [3] [6]. For example, triple-excited carbonyls are responsible for the emission in the wavelength range of 350–550 nm, singlet excited melanin with 360–560 nm, dimolar singlet oxygen with 634 nm and 703 nm, and monomolar singlet oxygen with 1270 nm [3].

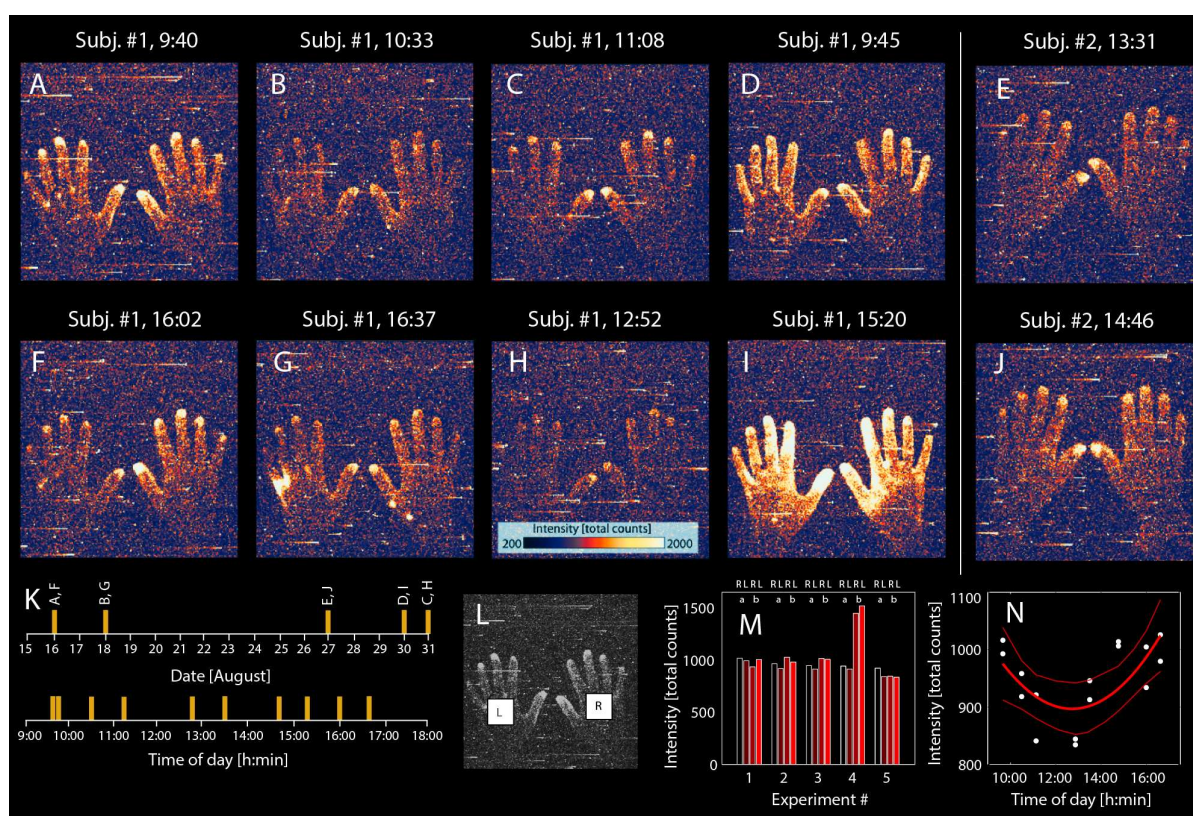
Autoluminescence has been detected from several living biological organisms like mice [8], rats [9], humans [10], cell cultures [11] and plants [12].

Due to its technical challenges, spatially-resolved (two-dimensional, 2D) UPE measurements on human body parts are currently done only by a few research groups worldwide. Initial work on human UPE imaging has been done since the 1990s by the Japanese research group of H. Inaba, demonstrating with a 2D photomultiplier setup that human hands show an inhomogeneous spontaneous UPE pattern with the highest intensity at the fingers and the lowest at the palm region [13] [14]. The group also found that sub-

jects with hypothyroidism had lower UPE values of their hands compared to a healthy control group [13] [14]. It was also observed that the UPE intensity at the right index finger in humans is generally higher than at the left one [9]. To obtain the UPE images, an exposure duration of 1 h has been used, illustrating clearly the extreme low intensity of the UPE detected. In the late 1990s, it was demonstrated for the first time that UPE images can be obtained from plants and animal tissue using a charge-coupled device (CCD) camera [9] [15]. Subsequent UPE imaging of human body parts with cryogenically cooled CCD cameras has been performed since the 2000s. Measurements on multiple body parts showed that a high UPE emission is detectable at the face and neck and that the hands exhibit a higher UPE intensity compared to the rest of the arm [16]. The next step in improving the technical setups to image human UPE was the usage of electron-multiplying CCD (EMCCD) cameras; first results were published in 2013 by the research group of R. van Wijk, E.P.A. van Wijk and J. van der Greef [10]. The UPE images of the hands showed a “high variability in emission intensity and pattern”. This study is a follow-up report on these measurements. Only a few reports of UPE EMCCD imaging have been published so far. A new development in UPE imaging is the realization of whole-body UPE counting and imaging of humans [17] [18] as well as the correlation of UPE images with metabolomics [19] [8] [20].

Objective

Our objective was to document and analyze a series of UPE images of hands obtained in 2011 by EMCCD imaging.



a

Figure Legend

Figure 1. EMCCD images of spontaneous UPE of human hands.

(A-J) UPE images of 2 subjects and 5 experiments (with 2 measurements per day). The information about the time of day when the images were made is given in the headers. Subject #1: A-C, F-H. Subject #2: E and J.

- (K) Visualization of the distribution of the dates and times of day when the UPE images were performed (5 different days, 10 different times of day).
- (L) ROIs used to calculate the mean UPE values for each of the 10 images. R: right, L: left.
- (M) Dependence of the mean UPE values (ROI, left and right hands) on experiment and subject. R: right, L: left, a: first measurement, b: second measurement.
- (N) Correlation of mean UPE values of subject #1 ($n = 16$) with the time of day ($r = 0.668$, $p = 0.0065$).

Results & Discussion

10 UPE hand images were obtained and analyzed in the present study (i.e. 8 images of subject #1, and 2 of subject #2). The following spatio-temporal aspects of the hand UPE images were noticed (Fig. 1): (i) all 10 images show clearly that human hands exhibit autoluminescence, i.e. spontaneous UPE; (ii) there was a large variability of the UPE intensity with respect to the factors time (time of day, date), anatomical location, and individual subject; (iii) images taken at the same date (but different times of day) showed a stronger similarity than images of the same subject taken on different dates.

Regarding the dependence of the UPE hand image features on the anatomy, the following aspect was observed: (i) the strongest UPE was measured generally at the fingers with the nails as the regions of maximal intensity; (ii) the nails of the thumbs exhibited generally especially large intensity values.

The mean intensity of the spontaneous UPE of the hands measured at regions of interest (ROIs) at the left and right hand were time-dependent. For subject #1, mean UPE values were quadratically correlated with the times of measurement ($n = 16$, $r = 0.668$, $p = 0.0065$), i.e. during noon minimal UPE values were recorded (Fig. 1N).

The mean intensity values from the ROIs were also dependent on the date. The lowest values were measured on August 31st, 2011, the highest on August 30th, 2011 (Fig. 1M). The UPE hand images of subject #2 were comparable to all 4 images of subject #2 with respect to anatomical characteristics of the UPE.

In 4 UPE images (Fig. 1A, B, F, G)) local increase in UPE intensity could be observed on the left hand at the skin between the fingers. At one instance a UPE “hot spot” at the left lateral side of the left hand can be seen (Fig. 1G) (the subject notices that this part of the skin was quite dry during the imaging); the right hand shows two “hot spots” too, but on the left lateral side (below the thumb).

The finding that hand UPE images exhibit a quite large variability of the intensity patterns with respect to the anatomy, subject and time, has been published [10]. Our finding in the current study that the nails and fingers exhibit the strongest UPE intensity of the hands, is in agreement with previous studies [16] [21]. The reason why the nails show a strong UPE is not fully understood. Possible explanations include differences in tissue, optical properties of tissue, microbial colonization or simply remaining dirt trapped in this area and causing delayed luminescence.

That the UPE intensity pattern varies strongly from day to day is an important finding in the current study. The time-dependence of UPE value from human body parts has been noticed already by previous investigations. In particular, Kobayashi et al. [22] reported that the mean UPE intensity measured from 5 subjects at the face and upper body parts showed a diurnal time-dependence with a peak in afternoon and the lowest values in the morning. This is partially in agreement with our observation of a peak of the hand UPE intensity in the afternoon. Kobayashi et al. [22] noticed also that the diurnal UPE intensity variation showed a statistically significant correlation with diurnal cortisol concentration fluctuations but not with body temperature. Cifra et al. [23] conducted 24 h measurements of spontaneous UPE of hands in humans and observed the same intensity pattern at the dorsum as we did: a decrease in intensity during noon and an increase in early afternoon. However, their inverse quadratic function fitted to the data is phase shifted by a few hours towards the evening as compared to our observed pattern. Concerning the inter-subject variability of UPE intensity from human hands, it was shown by Zhao et al. [24] that it can be explained to a large degree by the age of the subject. Since only UPE hand images of 2 subjects were investigated in our study, we could not test a possible age-correlation.

Conclusions

In this study, we presented examples of the feasibility of using an EMCCD camera to measure spontaneous ultra-weak photon emission (autoluminescence) from human hands. The image analysis revealed a large spatio-temporal variability of the UPE pattern correlations to anatomical locations and the time of measurement (especially the time of day).

The imaging of spontaneous UPE from human hands offers a new window into the (metabolic, compositional, hemodynamic) state of the tissue as well as possibly the state of the whole human subject. UPE imaging of hands (or even the whole body [17] [18]) might be a useful technique not only for basic research in human physiology and medical applications.

Since it is known that spontaneous UPE is correlated with the oxidative state of the tissue (oxidative stress) [25] [26], it would be very interesting for future studies to quantify the oxidative stress level at different parts of the hands and capture subsequently UPE images of them, enabling to analyze the correlation of both phenomena. Since there is also a correlation with local blood flow and tissue oxygenation with UPE [27], it would be of interest for future studies to analyze the correlation of the local microcirculatory state of hand tissue with UPE intensity.

Limitations

There are three main limitations to this study. First, only 2 subjects and only a quite small number ($n = 10$) of UPE images were analysed in the present study. A larger number would have made it easier to statistically investigate the dependence of the spatio-temporal characteristics of the UPE hand image patterns with several factors like the time of measurement (time of day, date) or individual subject. Second, the parallel measurement of additional local and systemic physiological parameters (like cortisol concentration, thermal image of the hand, microcirculation, melanin concentration, body temperature, heart rate, partial pressure of CO_2 in the blood, blood biomarkers of oxidative stress as well as O_2 , CO_2 and CO concentration of the air in the darkroom in combination with temperature, humidity and pressure in the darkroom) would have given additional insights into the origin of the spatio-temporal characteristics of the UPE hand image patterns. It has been shown already that the temperature of the hand is positively correlated with UPE intensity [21]. Third, a complete removal of cosmic ray artifacts in the UPE images was not conducted since there are no standard algorithms available to perform this task and an algorithm specifically dedicated to this task is currently still under development.

Additional Information

Methods and Supplementary Material

Please see <https://sciencematters.io/articles/201803000001>.

Ethics Statement

According to Medical Research Involving Human Subjects Act, this study did not require a medical ethics review. All subjects adequately understood the study procedure and gave their oral informed consent. The subjects measured were persons that were executing the experiments and writing the paper, i.e. no external subjects.

Citations

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